

REMARKS

This is in response to the Official Action of November 3, 2008. Applicants submit herewith a Request for Continued Examination. Applicants amend the principal independent claim to more particularly point out and distinctly claim that which applicants perceive to be their invention. Claim cancellations and amendments are made without prejudice or disclaimer.

The claims have been amended to more particularly and plainly recite the invention. Among other things, the method is now more succinctly claimed and recites generally producing microcapsules by solubilizing a plant protein in an aqueous medium at pH 2 - 7; centrifuging the solubilized plant protein to obtain a supernatant; mixing the supernatant with an aqueous polyelectrolyte solution wherein the polyelectrolyte has a charge opposite the plant protein; and coacervating the supernatant and polyelectrolyte mixture with a material to form a complex coacervate of the plant protein and the polyelectrolyte encapsulating the material. The material may be an active agent useful in pharmaceuticals, cosmetics, veterinary applications, agrofoods, and the like.

A significant advantage of the claimed invention is that it uses plant proteins in place of animal-derived proteins, thereby eliminating potential contamination by prions and other disease causing agents. Applicants distinguished the claimed invention over those requiring animal-derived constituents in the specification. *E.g.*, ¶¶ 0013-17, and 0021-22.

Another advantage is that the method is performed in an all aqueous medium, thereby avoiding the use of organic solvents, which pose problems in handling, removal, and disposal. Applicants described this feature as a particular advantage

and a distinguishing feature relative to other attempts to resort to plant proteins.

See, e.g., specification, ¶ 0018 -20 (distinguishing multi-phasic processes including Ezpeleta, Int. J. Pharm. (1996); and Perrier et al., WO99/03450 (and its priority case USPN 5,912,016)). None of the cited references offer the advantage of an all-aqueous system using proteins derived solely from plants.

To make the distinction more explicit, applicants submit herewith new claims 22-27, which, among other things, make explicit the distinction over the prior art that the claimed method is carried out in the absence of an organic solvent (e.g., ethanol) and any organic acid. Nonetheless, it is applicants' position that claim 21 and its dependent claims are patentable without those express distinctions. Accordingly, reconsideration and withdrawal of all outstanding rejections is respectfully requested.

Applicants' distinction over multi-phasic processes in the prior art in the Background section, and its numerous examples showing the use of a mineral acid rather than an organic acid amply support the new limitations of the new claims. *Ex Parte Parks*, 30 USPQ2d 1234, 1236 (BPAI 1993).

Prior Art Rejections

Claims stand rejected over Yajima JP 05-309261 ('261). As acknowledged, the '261 reference fails to teach or suggest substantial components of the claimed invention, including cationic polyelectrolytes and the use of glutaraldehyde as crosslinking agent for hardening the microcapsules.

The deficiencies of the '261 reference go beyond the acknowledged shortcomings. For example, the '261 reference requires the use of an organic component, e.g., ethanol (¶ 0005). The instant claims offer a substantial advantage

in facilitating the elimination of such organic components, and in the new claims such components are expressly excluded.

Likewise, the '261 reference acknowledges an advantage in reducing organic component in solubilizing plant protein, and states that objective can be achieved by resorting to the use of an organic acid. *See, e.g.*, ¶¶ 0004-5, 0009, and the Working Example. The '261 reference asserts that the organic acid is an essential component in a low ethanol solvent medium for extracting gluten. However, the reference does not teach or suggest that one can eliminate ethanol from the extraction medium, even in the presence of an organic acid. In any event, the reference teaches that both components (organic alcohol and organic acid) are essential to the successful use of the methods of the '261 reference.

As demonstrated in the instant Examples, the claimed methods are free of organic solvent and organic acid, and instead use mineral acid (e.g., HCl) to adjust pH. Moreover, the mineral acid is added after the plant protein has been solubilized in aqueous media. While it is true that certain claims do not expressly exclude organic solvent and/or organic acid, the instant specification shows that the claimed method can successfully be practiced without either component, and that successful complex coacervation can be achieved with a plant protein material in a distinct process. The '261 reference expressly teaches that such constituents are essential, and so it teaches away from the instant claims. Thus, the '261 reference fails to teach or suggest the claimed invention, and one skilled in the art would not have had any reasoned basis for resorting to the claimed methods, and would not have had any expectation of success even if they had such a basis.

Gillberg-LaForce (USPN 5,618,622, or "GL") fails to cure the deficiencies of the '261 reference. The rejection asserts that GL teaches polyelectrolytes that include chitosan and sodium carboxymethylcellulose. However, GL is nonanalogous art, and there has been no showing that one skilled in the art seeking to make microcapsules by complex coacervation would have turned to GL for any teaching, much less that relied on here; nor has there been any showing that one skilled in the art would have combined the particular statements and/or reagents of GL with those of the '261 reference, or that they would have done so in such a way as to arrive at the claimed subject matter.

GL is directed to a "surface-modified fibrous material." The material is said to be useful in the manufacture of a filter medium in "depth-type filters." Among other things, the GL disclosure allegedly provides "means by which polyelectrolytes may be incorporated into a depth filter thereby endowing the fibers with the potential for affinity filtration." Col. 3, lines 3-5.

Although the GL reference refers to polyelectrolytes, there has been no showing that the reference teaches or suggests the suitability of such polyelectrolytes in anything resembling a coacervation process, much less a complex coacervation process, and particularly not one using a plant protein in an all aqueous phase process.

Further, GL does not teach or suggest that any of its recited polyelectrolytes would have facilitated a complex coacervation process involving solubilization of a plant protein in an all aqueous medium at pH 2-7; centrifugation; addition to the resulting supernatant of a polyelectrolyte of opposite charge to the plant protein; and a complex coacervation step to encapsulate a material. In short, GL does not teach

or suggest that it's disclosed polyelectrolytes would have allowed the development of complex coacervation using plant protein based microcapsules in an all aqueous medium and free of organic acid.

Nor does Ezpeleta eliminate the deficiencies of the '261 reference and/or GL. It is asserted that Ezpeleta teaches the formation of nanoparticles from gliadin (a vegetal protein fraction from wheat gluten); and that chemical cross-linkage of nanoparticles with glutaraldehyde significantly increased the stability of the gliadin nanoparticles. It is further asserted that Ezpeleta teaches that using plant proteins can be used in producing nanoparticles for incorporating a wide variety of drugs. Nonetheless, the rejection fails to show that one of ordinary skill in the art would have combined the teachings of Ezpeleta, such as they are, with those of '261 and GL to arrive at the claimed methods.

Ezpeleta states that the gliadin nanoparticles are prepared by a desolvation method wherein the plant protein is dissolved in an organic solvent/water phase, and extracted in the solvent phase, which is subsequently added to a physiological saline phase with a Synperonic PE/F 68 stabilizer. The organic solvent was then removed by evaporation. Ezpeleta, p. 193.

Ezpeleta does not teach or suggest that the use of glutaraldehyde in an effort to cross-link particles resulting from those organic phase fabrication processes could have facilitated an all-aqueous fabrication method. Likewise, Ezpeleta does not teach or suggest that the '261 method can be practiced free of organic solvent and/or organic acid - with or without resort to glutaraldehyde; and likewise, it does not teach or suggest that its methods and/or reagents can be employed to benefit in a method such as that of the '261 method, and, even if it did, it does not state which of those

methods or reagents can be so employed. There has been no showing that Ezpeleta's use of glutaraldehyde would have suggested in any way to one of ordinary skill in the art that the need for ethanol and/or organic acid as taught in the '261 reference is eliminated. Indeed, Ezpeleta own use of an organic phase supports and strengthens the teaching of the '261 reference with regard to the need for organic solvent in the fabrication process.

Ezpeleta does not cure the deficiencies of the '261 reference, and it does not teach or suggest the claimed invention, alone or in combination with either or both of the '261 reference and/or the GL reference. Accordingly, the cited references do not teach or suggest the claimed invention, and applicants respectfully request further examination, and reconsideration and withdrawal of all rejections.

In view of the foregoing, the subject matter of the independent claims would not have been obvious over the combination of the '261 reference, GL, and Ezpeleta. And because the subject matter of the independent claims would not have been obvious, it likewise stands that the subject matter of dependent claims 5-6 would not have been obvious in view of those references in combination with Kangas et al.

Kangas is also non-analogous art. Kangas is directed to the preparation of materials useful in., among other things, sewage treatment, the separation of sludges, and the fabrication of "dipped goods." It involves as a stated advantage, the "latent gelation of foamed and non-foamed, anionically-stabilized latexes of water-insoluble organic polymers." Col. 3, lines 1-19.

It has not been shown that the reference teaches or suggests, or that one skilled in the art would have inferred, that any of its teachings are applicable to the fabrication of complex coacervates wherein plant protein is used to encapsulate

materials such as therapeutically effective agents. Nor is there any teaching or suggestion that such complex coacervates can be made in an aqueous medium free of organic solvent and/or organic acid. Accordingly, Kangas fails to cure the deficiencies of the '261 reference, GL, or Ezpeleta, with regard to the independent claims, and particularly with regard to claims 5-6. Reconsideration and withdrawal of the rejection is respectfully requested.

Finally, the subject matter of claim 14 is not suggested by the combination of the '261 reference, GL, Ezpeleta and Lee. As shown above, the subject matter of the independent claims, and the dependent claims other than claim 14 are neither taught nor suggested by the '261 reference, GL, and Ezpeleta (and/or Kangas). Accordingly, the subject matter of a dependent claim is likewise not obvious over those references, separately or in combination with Lee. And, as above with Kangas, Lee fails to cure the deficiencies of those references.

It is asserted that Lee teaches hardening microcapsules containing chitosan by using acetic anhydride. However, it is not asserted nor is it shown that Lee cures the other deficiencies of the cited references. Thus, there is no showing that Lee combines with the other cited references to suggest a complex coacervation method using plant protein in combination with another polyelectrolyte in an all-aqueous medium. Accordingly, the subject matter of claim 14, and all other claims, is neither taught nor suggested by the combination of the '261 reference, GL, Ezpeleta, and Lee. Applicants respectfully request reconsideration and withdrawal of this and all other outstanding rejections.

Conclusion

In view of the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of all outstanding rejections. Applicants submit that the claims are now in condition for allowance, and respectfully request formal notification to that effect. If, however, the Examiner perceives any impediments to such a notice of allowability, whether substantive or formal, the Examiner is encouraged to call Applicants' attorney at the number provided below. Such informal communication will expedite examination and disposition of this case.

Respectfully submitted,

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